Mycolactone Gene Expression Is Controlled by Strong SigA-Like Promoters with Utility in Studies of Mycobacterium ulcerans and Buruli Ulcer

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Résumé en anglais	Buruli ulcer (BU) is a serious skin infection of humans predominantly occurring in West and Central Africa. The disease is caused by infection with Mycobacterium ulcerans, a bacterium that produces an unusual toxin called mycolactone. There are many unanswered questions surrounding BU, particularly regarding the role of mycolactone in disease and how M. ulcerans is transmitted to humans. Here, we have partly addressed these questions by identifying genetic factors controlling the transcription of the mycolactone genes. Using a variety of experimental approaches, including green fluorescent protein (GFP) as a reporter of gene expression, we have identified strong promoters that drive transcription of the mycolactone genes in M. ulcerans. We then used our GFP reporters to produce highly fluorescent M. ulcerans-GFP that were readily visualized by microscopy. Mosquitoes have been proposed as a potential vector of M. ulcerans so we used M. ulcerans-GFP in feeding experiments with mosquito larvae. M. ulcerans-GFP accumulated within the insects, whereas other mycobacteria did not. This is the first report of the mycolactone gene promoters, and we have used our findings to develop M. ulcerans-GFP, a strain in which fluorescence and toxin gene expression are linked, thus providing a powerful tool for studying Buruli ulcer.
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